Appendix 3: Description of randomized trials of therapy for diastolic heart failure (part 1 of 2)

Study, sample size, study design*	Description of intervention	Control(s)	Inclusion criteria	Definition of diastolic dysfunction	Age, yr	Mean LVEF, %	Gender, % women	Setting
ACE inhibitors, angiotensin-receptor blockers								
Cleland et al, PEP-CHF, (n = 850), RCT[27]	perindopril (titrated)	placebo	age ≥ 70, CV hospitalization within past 6 months,	LVEF ≥ ~40%,† clinical + echo criteria	75	64	56	Europe
Zi et al (n = 74), RCT[28]	quinapril, (titrated)	placebo		LVEF ≥ 40%	78	59	65	Two UK hospitals
Lang et al (n = 12), RCT with crossover[30]	lisinopril (titrated)	placebo		LVEF > 50%, echo diastolic dysfunction	72	NS	58	One UK hospital
Aronow et al (n = 21), RCT[31]	enalapril (titrated)	allowed furosemide	previous myocardial infarction.	LVEF > 50%	80	64	86	New York City, US
Yip et al (n = 151), RCT[29]	irbesartan (titrated) v. ramipril (titrated))	conventional	clinical history of heart failure within 2 months of screening	LVEF > 45%	74	67	62	Hong Kong
Yusuf et al, CHARM-preserved (n = 3023), RCT[32]	candesartan (titrated)	placebo	previous hospital admission for a cardiac reason	LVEF > 40%	67	54	40	618 centres in 26 countries
Beta blockers								
Aronow et al (n = 158), RCT[34]	propranolol (titrated)	conventional therapy	previous myocardial infarction.	LVEF ≥ 40%	81	56	71	not specified
Takeda et al (n = 40), RCT[35]	carvedilol (titrated)	conventional therapy		LVEF ≥ 45%	71	57	48	1 clinic in Japan
Flather et al, SENIORS (total n = 2128, DHF n = 752), RCT[33]	nebivolol (titrated)	placebo	age ≥ 70, recent heart failure admission within 12 months	LVEF > 35%‡	76	NS	37	multicenter, international, 11 European countries
Other pharmacologic therapies								
Hung et al (n = 15), RCT with crossover[37]	Calcium-channel blocker: verapamil 120 mg/day	placebo		LVEF > 50% and echo criteria	65	70	40	Taiwan

Appendix 3: Description of randomized trials of therapy for diastolic heart failure (part 2 of 2)

Study, sample size, study design*	Description of intervention	Control(s)	Inclusion criteria	Definition of diastolic dysfunction	Age, yr	Mean LVEF, %	Gender, % women	Setting
Ahmed et al, DIG ancillary (*n* = 988) , RCT[36]	digoxin 0.125 mg/day, 0.25 mg/day, 0.375 mg/day or 0.5 mg/day	placebo		LVEF > 45%	67	56	41	US, Canada
Cohn et al, Vheft (*n* = 83) , RCT[38]	isosorbide dinitrate 40 mg QID and hydralazine 75 mg QID v. prazosin 5 mg QID	placebo	Male with cardiac enlargement or dilated left ventricle and exercise intolerance	LVEF ≥ 45%	60	54	0	11 Veteran Affairs hospitals in US
Nonpharmacologic therapies								
Galbreath et al (total *n* = 1,069, DHF *n* = 317), RCT[43]	disease management program	usual care		LVEF ≥ 50%, echo criteria	71	62	29	center in Texas
Gary et al (*n* = 32) , RCT[39–41]	12 week walking program	education only	women, ≥ 50 years old	LVEF ≥ 45%, had a diagnosis of diatolic dysfunction or DHF	68	55	100	University of North Carolina, US

Note: ACE = angiotensin-converting-enzyme inhibitor, RCT = randomized controlled trial, DHF = diastolic heart failure, LVEF = left ventricular ejection fraction, echo = echocardiogram, CV = cardiovascular.
*References are available in the main text of the article (www.cmaj.ca/cgi/content/full/180/5/520).
†Original trial used wall motion index cutoff of 1.4 which is roughly equivalent to LVEF of 40%.
‡Patients were included if LVEF >35%, but for the non-prespecifed combined outcome, a LVEF cutoff of 40% was used.